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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,509	12/07/2001	Maric-Claude Gingras	HO P02046US1	8559

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,509	GINGRAS ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 9-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 05/27/04 is acknowledged.

Claims 1, 3-7 and 9 -17 are pending.

Claims 1, 3-7 and 9 -17 drawn to a method of modulating an immune response; a method of decreasing myeloid cell activation and a method of modulating an inflammatory response each comprising the step of administering a compound to an animal to decrease the activity of DAP12/TREM-1 complex are under consideration in the instant application.

In view of the amendment, filed 05/27/04 the following rejections remain:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 3-7 and 9 -17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons set forth in the previous Office Action, mailed 2/27/04.

Applicant's arguments, filed 05/27/04 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) the invention need not be reduced to practice prior to filing; (ii) the Examiner required a human trials as the only sufficient support for enablement and that clinical testing is not required to obtain a patent; (iii) Declaration under 37 CFR 1.132 by one of the inventors Dr. Gingras stated that specification provided sufficient guidance for those skill in the art to perform the claimed invention; (iv) Bouchon et al (Nature ,2001, 410 1103-1107) reference utilized the teaching of the present invention, thus showing the enablement of the present invention.

Contrary to Applicant's assertion, in the previous Office Action the was no requirement for a human trials as the only sufficient support for enablement. The issue raised in the previous Office Action was that the specification only discloses: (i) the levels of TREM-1 expression in various tissues and cell types (see Examples 4 and 5 in particular); (ii) the levels of TREM-1 splice variant, in samples collected from normal individuals and individual suffering from an autoimmune disease (see example 10 in particular); (iii) *in vitro* data indicating that TREM-1 splice variant, a polypeptide comprising SEQ ID NO:2 can down regulate LPS-induced cytokine production (see example 11 in particular); (iv) a competitive inhibitor for the ligand of TREM-1, wherein said competitive inhibitor is a polypeptide comprising SEQ ID NO:2 (see page 14 in particular). The specification does not adequately teach how effectively modulate an immune response or decrease myeloid cell activation or modulate an inflammatory response by administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof. Moreover, no animals models were used to study the effectively to modulate an immune response or to decrease myeloid cell activation or to modulate an inflammatory response by administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1, or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof. The specification only states that it is envisioned that administering of TREM-1 splice variant may resulting down regulation of the inflammatory response (see page 45 in particular). Similarly, the Declaration under 37 CFR 1.132 by Dr. Gingras stated that the inventors envisioned modulating inflammation in septic shock by administering a competitive inhibitor of the ligand for TREM-1 (see page 1 in particular). In addition, Bouchon et al (Nature ,2001, 410 1103-1107) reference only teaches a very specific mTREM-1/IgG1 fusion protein, not *any* compound that was used in experimental endotoxic shock and can reduces not modulate inflammatory responses. The claimed "modulating an immune response"" would be interpreted by one skilled in the art as mutually exclusive in that they reach opposing endpoints, and in that they employ structurally distinct "agents" to accomplish these mutually exclusive endpoints.

Since there is no animal model studies and data in the specification to show the effectively of modulating an immune response or decreasing myeloid cell activation or modulating an inflammatory response by administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof it is unpredictable how to correlate *in vitro* results with *in vivo* use. Bouchon et al., (IDS) teaches that distinct TREM receptors are involved in regulation of various types of immune responses including acute and chronic inflammatory responses (see entire document, page 4995 in particular). Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". Feldman et al . further teach that in a chronic immune-driven inflammatory response

there are a number of pathways that become engaged and effective therapy in immune inflammatory diseases such as rheumatoid arthritis, will come from therapy aimed at several points in the disease pathway. In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to *in vitro* models, and partly animal-human xenograft systems, tissue cells *in vivo* seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail in vivo. Since a method of modulating an immune response or a method of decreasing myeloid cell activation or a method of modulating an inflammatory response each comprising administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1, or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof can be species- and model-dependent (see Van Noort et al. International Review of Cytology, 1998, v.178, pages 127-204, Table III in particular) , it is not clear that reliance on the *in vitro* studies accurately reflects the relative mammal and human efficacy of the claimed therapeutic strategy. Van Noort et al. further indicates factors that effect immune response such as genetic, environmental and hormonal (Page 176, Paragraph 3). The ability of a host to enhance an immune response will vary depending upon factors such as the condition of the host and burden of disease. The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective *in vivo* mammalian including human therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of modulating an immune response or a method of decreasing myeloid cell activation or a method of modulating an inflammatory response each comprising administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 ,or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof. Thus in the absence of working examples or detailed guidance in the specification, the intended *in vivo* uses of an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 ,or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof to modulate an immune response or to decrease myeloid cell activation or to modulate an inflammatory response are fraught with uncertainties.

It addition, an effective protocol to modulate an immune response or to decrease myeloid cell activation or to modulate an inflammatory response each comprising administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 ,or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof in the absence of *in vivo* clinical data are unpredictable for the following reasons: (1) the polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the polypeptide may not reach the target area because, it may not be able to cross the mucosa or the polypetide may be adsorbed by fluids, cells and tissues where the polypetide has no effect; and (3) other functional properties, known or

unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Also an issue that applicant has not taught how to make and/or use *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 ,or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof to effectively modulate an immune response or decrease myeloid cell activation or modulate an inflammatory response. The structural and functional characteristics of said *any* compound or *any* functional equivalent of a polypeptide comprising the amino acid sequence of SEQ ID NO:2 are not defined in the claim.

"Comprising" is considered open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, a peptide comprising the amino acid sequence of SEQ ID NO:2 includes an unlimited number of amino acid sequences "comprising" an unlimited number of polypeptides. The disclosure of SEQ ID NOS: 2 cannot support the entire genus of peptides comprising the amino acid sequence of SEQ ID NO:2 as part of their sequence .

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated " *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 ,or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof" encompassed by the claimed invention other than "a polypetide consisting the amino acid sequence of SEQ ID NO: 2" would be expected to have greater differences in their activities.

Applicant has not provided sufficient biochemical information (e.g. structural characteristics, amino acid composition , physicochemical properties, etc) that distinctly identifies *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 ,or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof other than polypeptide consisting the amino acid sequence of SEQ ID.NO.2 While any "*any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 or any functional equivalent of the amino acid sequence of SEQ ID NO.2" may have some notion of the activity of the "a polypeptide consisting the amino acid sequence of SEQ ID NO.2", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of

representative compounds falling within the scope of the instant claims and consequently would not know how to make them.

Protein chemistry is probably one of the most unpredictable areas of biotechnology . It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular). Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the poplypetide to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions.

Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. modulate an immune response or decrease myeloid cell activation or modulate an inflammatory response) requires a knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain functional aspects the peptides and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional proteins or peptides with the desired properties and that the relationship between the sequence of a peptide and it's tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention. Without sufficient guidance, the changes which can be made in the structure

of "cyclic peptide" and still specifically blocks the interaction of CD4 and MHC class II, gene products is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

It is noted that Applicant has not addressed that issue.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of modulating an immune response or method of decreasing myeloid cell activation or method of modulating an inflammatory response each comprising administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 , or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. Claims 1, 3-7 and 9 -17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, mailed 2/27/04.

Applicant's arguments, filed 05/27/04 have been fully considered, but have not been found convincing.

Applicant asserts that one skilled in the art would be able to follow the guidance in the specification to found and produce compounds that would result in the desired function.

Contrary to Applicant's assertion, the claimed invention is drawn to genus of compound to decrease myeloid cell activation. However, no structural characteristics of such compounds is provided. A description of a protein by functional language in the absence of a structure is not considered sufficient to show possession of the claimed invention. See Fiers, 984 F.2d at 1169-71, 25 USPQ2D at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many species may achieve that result. The definition requirement of the patent statute requires a description of an invention, not an indication of a result that one

might achieve if one made that invention. See In re Wilder, 736 /f.2d 1516, 1521, 22 USPQ 369, 372-73 (Fed. Cir. 1984) affirming the rejection because the specification does "little more than outline[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of (e.g. structural feature), is not a description of that material.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for finding a product is not equivalent to a positive recitation of how to make a product.

Applicant is not in possession of : a method of modulating an immune response or a method of decreasing myeloid cell activation or a method modulating an inflammatory response in the subject each comprising administering an effective amount of *any* compound to decrease myeloid cell activation , or *any* compound that is an competitive inhibitor of the ligand to TREM-1 or a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a functional equivalent thereof.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of what a material does rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

A description of a genus of compound to decrease myeloid cell activation may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1, 3-7 and 9 -17 stand rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,420,526 or US Patent 6,504,010 forth in the previous Office Action, mailed 2/27/04.

Applicant's arguments, filed 05/27/04 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) he did not receive the sequence alignment mention by the Examiner; (ii) at best US Paten '526 teaches a sequence similar to TREM or SEQ ID NO:1 that may be involved in the activation of neutrophils, however it does not teach that competitively inhibiting the ligand for TREM-1 or SEQ ID NO:1; (iii) although US Patent ''010 teaches a sequence similar to TREM or SEQ ID NO:1 it does not teaches a decreasing an immune response or myeloid cell activation.

Contrary to Applicant's assertion, it is noted that SEQ ID NO: 1, mention by the Applicant is DNA sequence, not a protein sequence thus it can not be similar to protein sequences taught by either US Patent '526 or US Patent '010. However, the sequence alignment, shown that polypeptide comprising SEQ ID NO:2 of the instant application is 100 % identical to SEQ ID NO: 478 of US Patent '526 or 100 % identical to SEQ ID NO: 1825 of US Patent '010 is inclosed. Also, applicant relies upon an asserted and claimed mechanism of action but does not provide objective evidence that the prior art teaching of administering of polypeptide that is

identical to the claimed polypeptide comprising SEQ ID NO:2 to achieve the same therapeutic effect differs from the claimed methods.

As was stated in the previous Office Action, US Patent '526 teaches a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 478 in a pharmaceutical carrier (see entire document , abstract, columns 4, 8 ,77 in particular). It is noted that SEQ ID : 2 of the instant application is 100 % identical to SEQ ID NO: 478 of US Patent '526 (see attached sequence alignment) . US Patent '526 teaches that disease are infectious disease, GVHD and septic shock (see column 77 and 132 in particular). Although the reference is silent about decreasing the activity of DAP12/TREM1 complex after administering of SEQ ID NO: 478, or that SEQ ID NO: 478 is a competitive inhibitor of the ligand to TREM-1 these functional limitations would be inherent properties of said polypeptide because it is 100 % identical with the claimed SEQ ID NO:2. Since the office does not have a laboratory to test the reference polypeptide, it is applicant's burden to show that the reference polypeptide does not decrease the activity of DAP12/TREM1 complex or not a competitive inhibitor of the ligand to TREM-1 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claims 6, 7-11 and 17 are included because the claimed functional limitation would be inherent properties of the a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 478 taught by US Patent '526 because the referenced polypeptide of SEQ ID : 478 used in the referenced methods is 100 % identical with the claimed SEQ ID NO:2 used in the claimed methods. It is clear that US Patent '526 and the current application administered the same compound to achieved the same results in the same patients thus the reference polypeptide would inherently performed the intended use. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. polypeptide of SEQ ID NO: 478) and the use is directed to a result or property of that composition or structure then the claim is anticipated. In addition, under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02 . Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Similarly, US Patent '010 teaches a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 1825 in a pharmaceutical carrier (see entire document , abstract, column3 45, 46, 78 and 79 in particular). It is noted that SEQ ID :2 of the instant application is 100 % identical to SEQ ID NO: 1825 of US Patent '010 (see attached sequence alignment). Although the reference is silent about decreasing the activity of DAP12/TREM1 complex after administering of SEQ ID NO: 1825, or that SEQ ID NO: 1825 is a competitive inhibitor of the ligand to TREM-1 these functional limitations would be inherent properties of said polypeptide because it is 100 % identical with the claimed SEQ ID NO:2. Since the office does not have a laboratory to test the reference polypeptide, it is applicant's burden to show that the reference polypeptide does not decrease the activity of DAP12/TREM1 complex or not a competitive inhibitor of the ligand to TREM-1 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claims 6, 7-11 and 17 are included because the claimed functional limitation would be inherent properties of the a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 1825 taught by US Patent '010 because the referenced polypeptide of SEQ ID : 010 used in the referenced methods is 100 % identical with the claimed SEQ ID NO:2 used in the claimed methods. It is clear that US Patent '010 and the current application administered the same compound to achieved the same results in the same patients thus the reference polypeptide would inherently performed the intended use. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. polypeptide of SEQ ID NO: 1825) and the use is directed to a result or property of that composition or structure then the claim is anticipated. In addition, under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02 . Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

As pointed out previously, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which a particular compound decrease myeloid cell activation it does not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same endresult. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

The reference teaching anticipates the claimed invention.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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July 6, 2004

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